FIG. 1

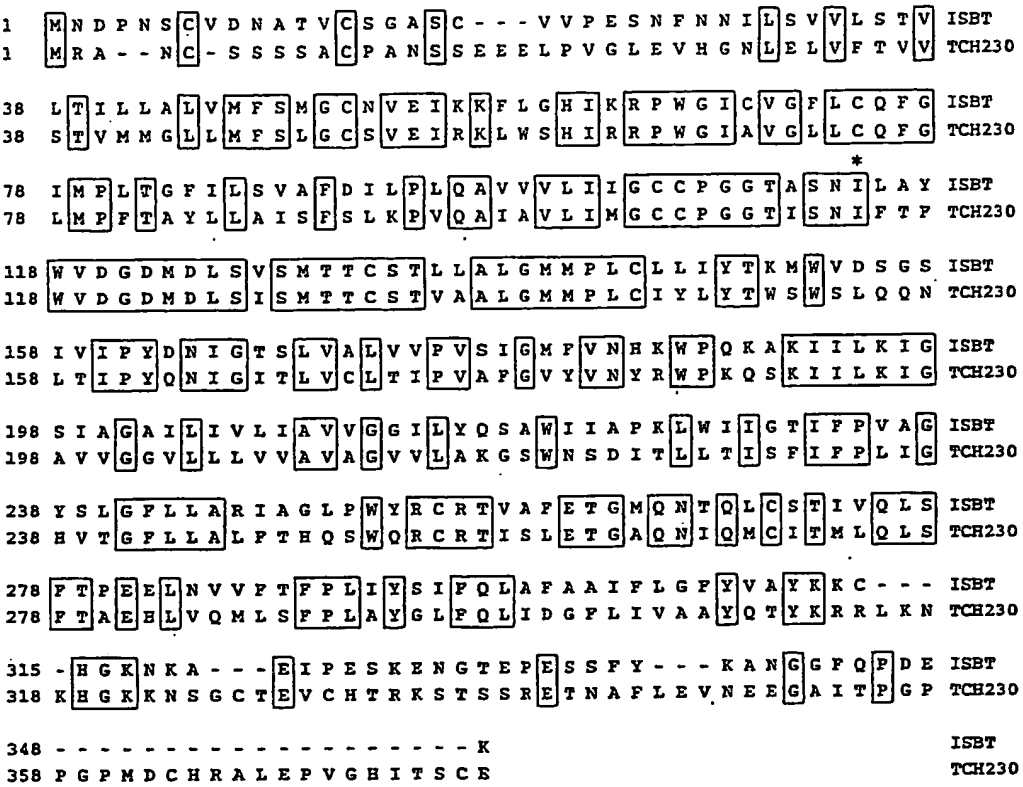

1 MNDPNSCVDNATVCSGASC---VVPESNFNNILSVVLSTV ISBT
1 MRA--NC-SSSSACPANSSEEELPVGLEVHGNLELVFTVV TCH230
38 LTILLALVMFSMGCNVEIKKFLGHIKRPWGICVGFLCQFG ISBT
38 STVMMGLLMFSLGCSVEIRKLWSHIRRPWGIAVGLLCQFG TCH230
78 IMPLTGFILSVAFDILPLQAVVVLIIGCCPGGTASNI* LAY ISBT
78 LMPFTAYLLAISFSLKPVQAIAVLIMGCCPGGTISNIFTF TCH230
118 WVDGDMDLSVSMTTCSTLLALGMMPLCLLIYTKMWVDSGS ISBT
118 WVDGDMDLSISMTTCSTVAALGMMPLCIYLYTWSWSLQQN TCH230
158 IVIPYDNIGTSLVALVVPVSIGMFVNHKWPQKAKIILKIG ISBT
158 LTIPYQNIGITLVCLTIPVAFGVYVNYRWPKQSKIILKIG TCH230
198 SIAGAILIVLIAVVGGILYQSAWIIAPKLWIIGTIFPVAG ISBT
198 AVVGGVLLLVVAVAGVVLAKGSWNSDITLLTISFIFPLIG TCH230
238 YSLGFLLARIAGLPWYRCRTVAFETGMQNTQLCSTIVQLS ISBT
238 HVTGFLLALFTHQSWQRCRTISLETGAQNIQMCITMLQLS TCH230
278 FTPEELNVVFTFPLIYSIFQLAFAAIFLGFYVAYKKC--- ISBT
278 FTAEHLVQMLSFPLAYGLFQLIDGFLIVAAYQTYKRRLKN TCH230
315 -HGKNKA---EIPESKENGTEPESSFY---KANGGFQPDE ISBT
318 KHGKKNSGCTEVCHTRKSTSSRETNAFLEVNEEGAITPGP TCH230
348 ----------K ISBT
358 PGPMDCHRALEPVGHITSCE TCH230

FIG. 2

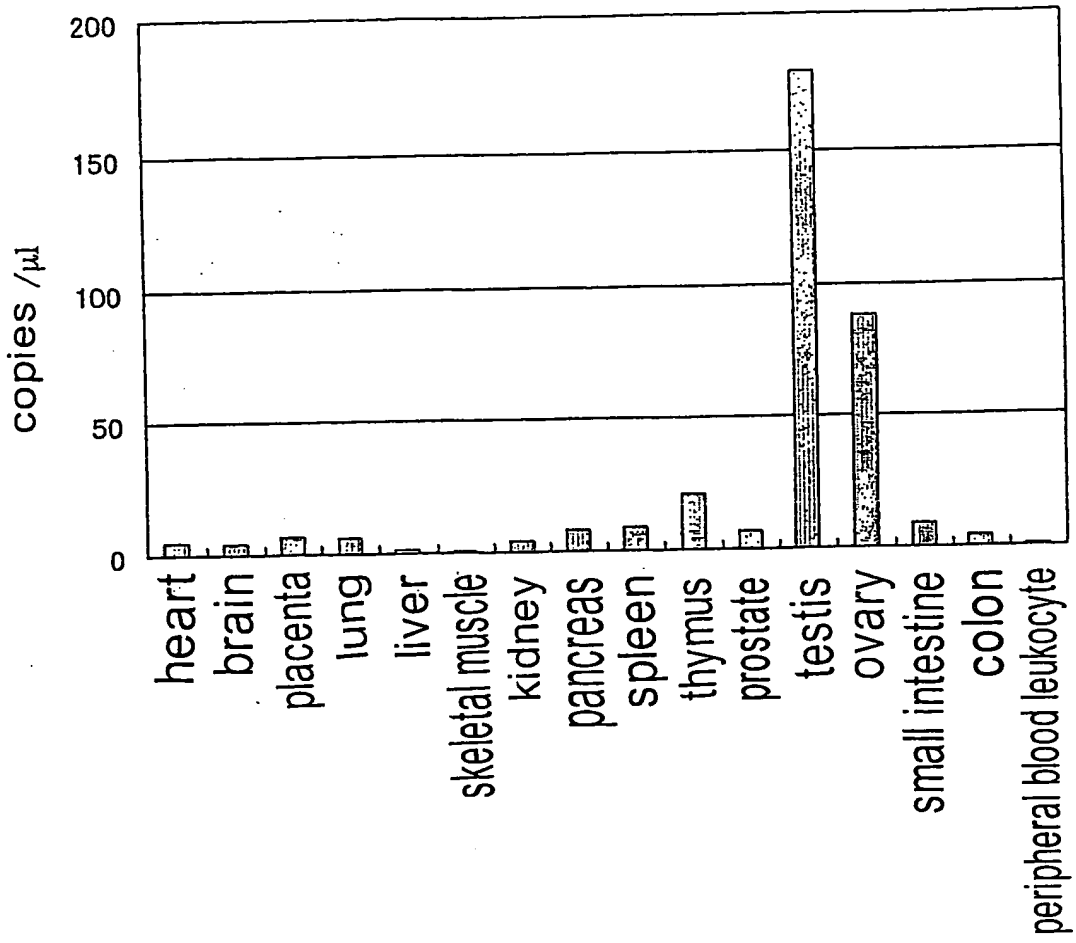

200
150
100
50
0
copies /μl
heart
brain
placenta
lung
liver
skeletal muscle
kidney
pancreas
spleen
thymus
prostate
testis
ovary
small intestine
colon
peripheral blood leukocyte

FIG. 3

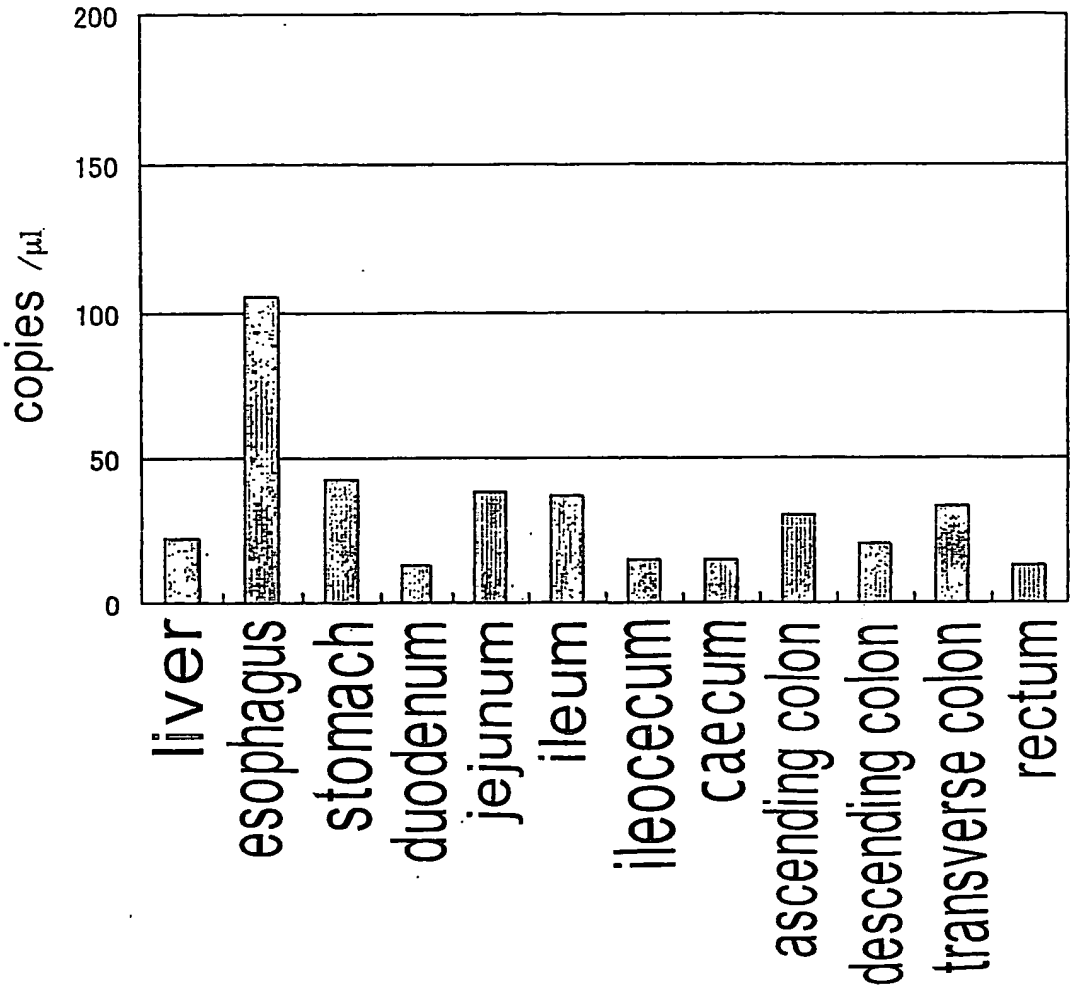

200
150
100
50
0
copies /μl
liver
esophagus
stomach
duodenum
jejunum
ileum
ileocecum
caecum
ascending colon
descending colon
transverse colon
rectum

FIG. 4

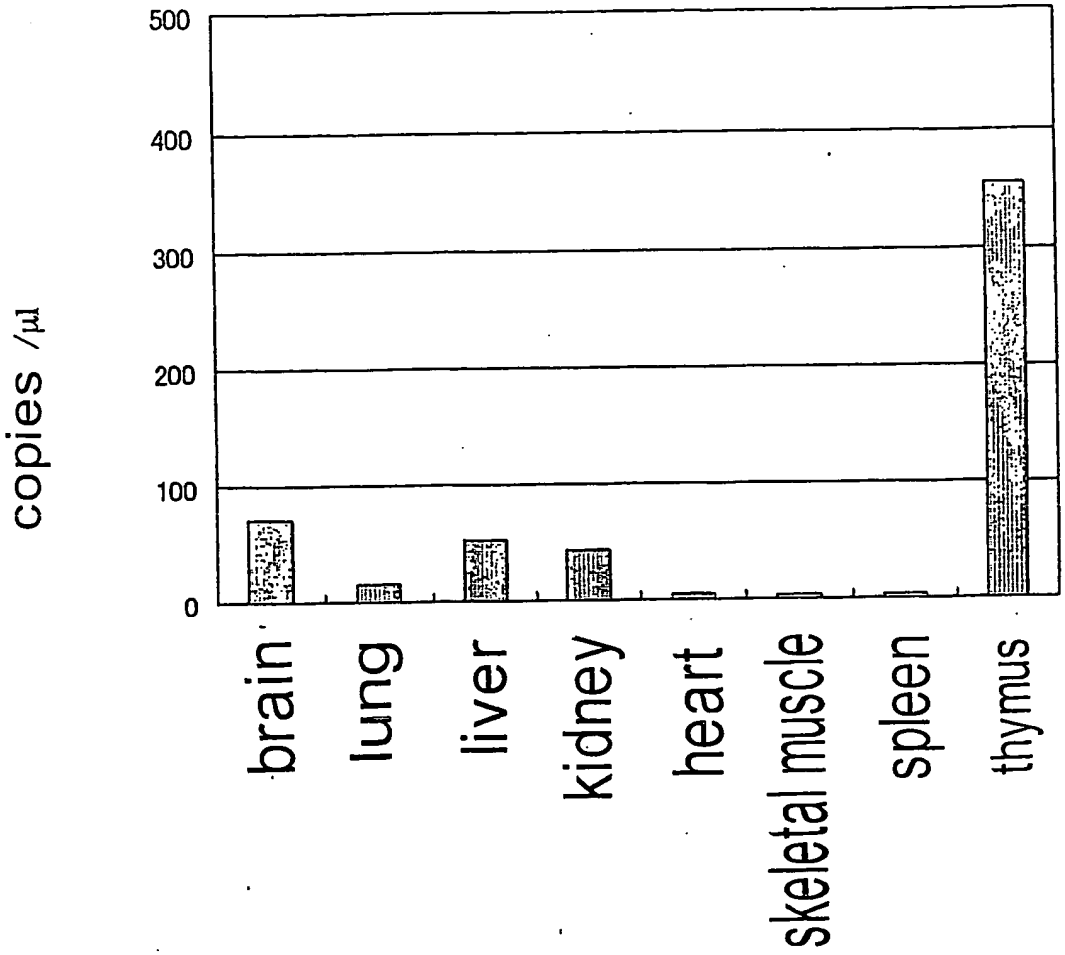

copies /μl
500
400
300
200
100
0
brain
lung
liver
kidney
heart
skeletal muscle
spleen
thymus

FIG. 5

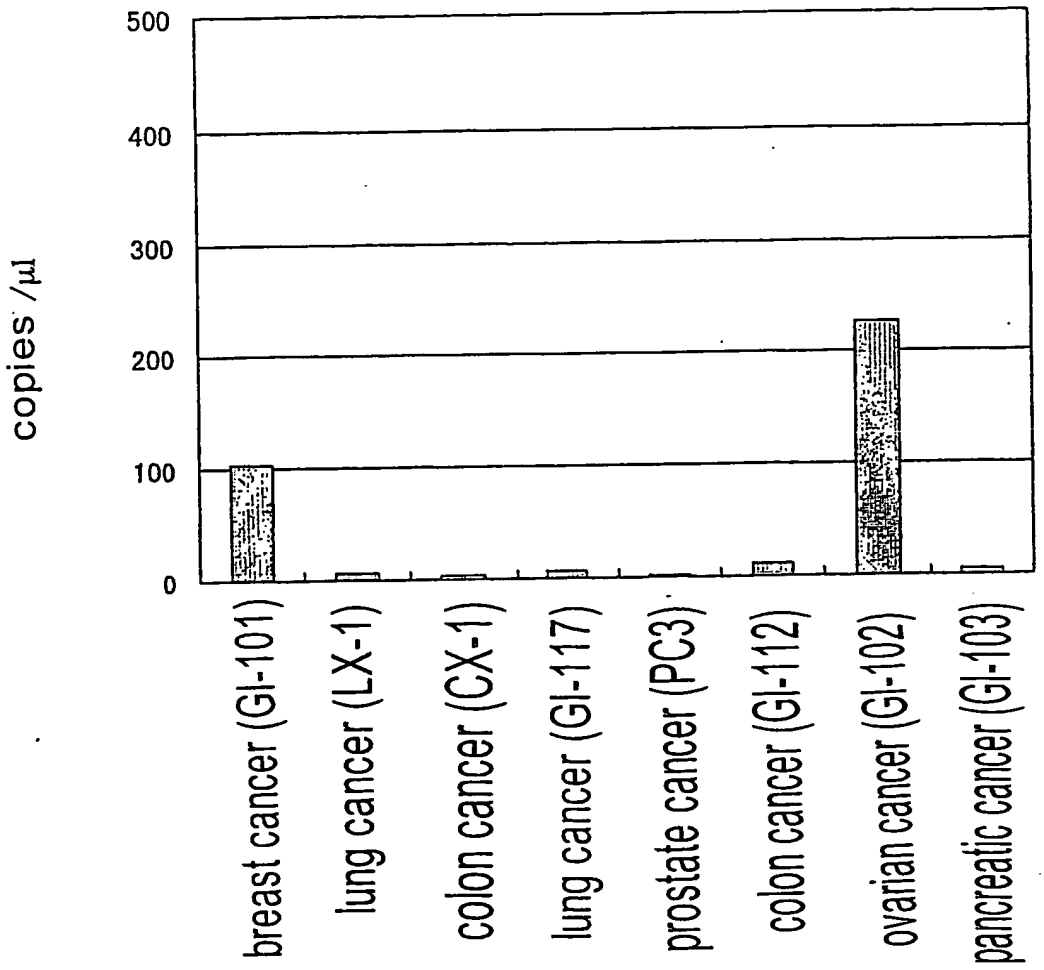

copies /μl
500
400
300
200
100
0
breast cancer (GI-101)
lung cancer (LX-1)
colon cancer (CX-1)
lung cancer (GI-117)
prostate cancer (PC3)
colon cancer (GI-112)
ovarian cancer (GI-102)
pancreatic cancer (GI-103)

FIG. 6

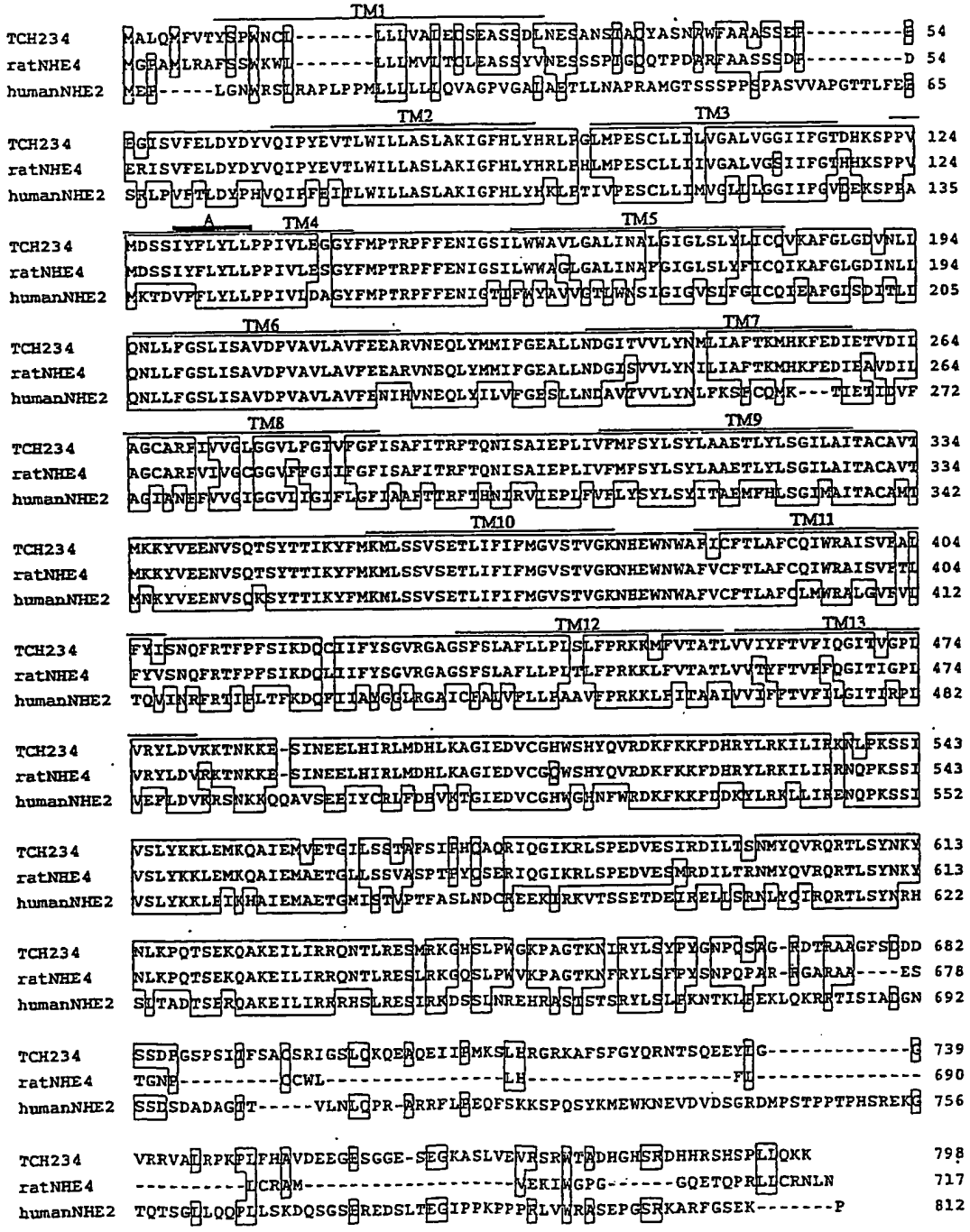

TM1
TM2
TM3
A
TM4
TM5
TM6
TM7
TM8
TM9
TM10
TM11
TM12
TM13
TCH234
ratNHE4
humanNHE2

FIG. 7

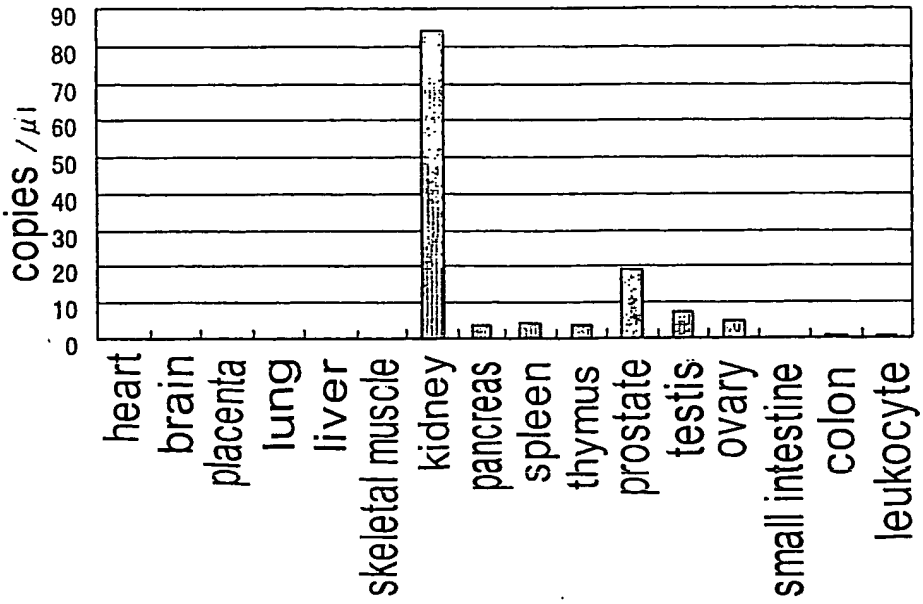

copies /μl
90
80
70
60
50
40
30
20
10
0
heart
brain
placenta
lung
liver
skeletal muscle
kidney
pancreas
spleen
thymus
prostate
testis
ovary
small intestine
colon
leukocyte

FIG. 8

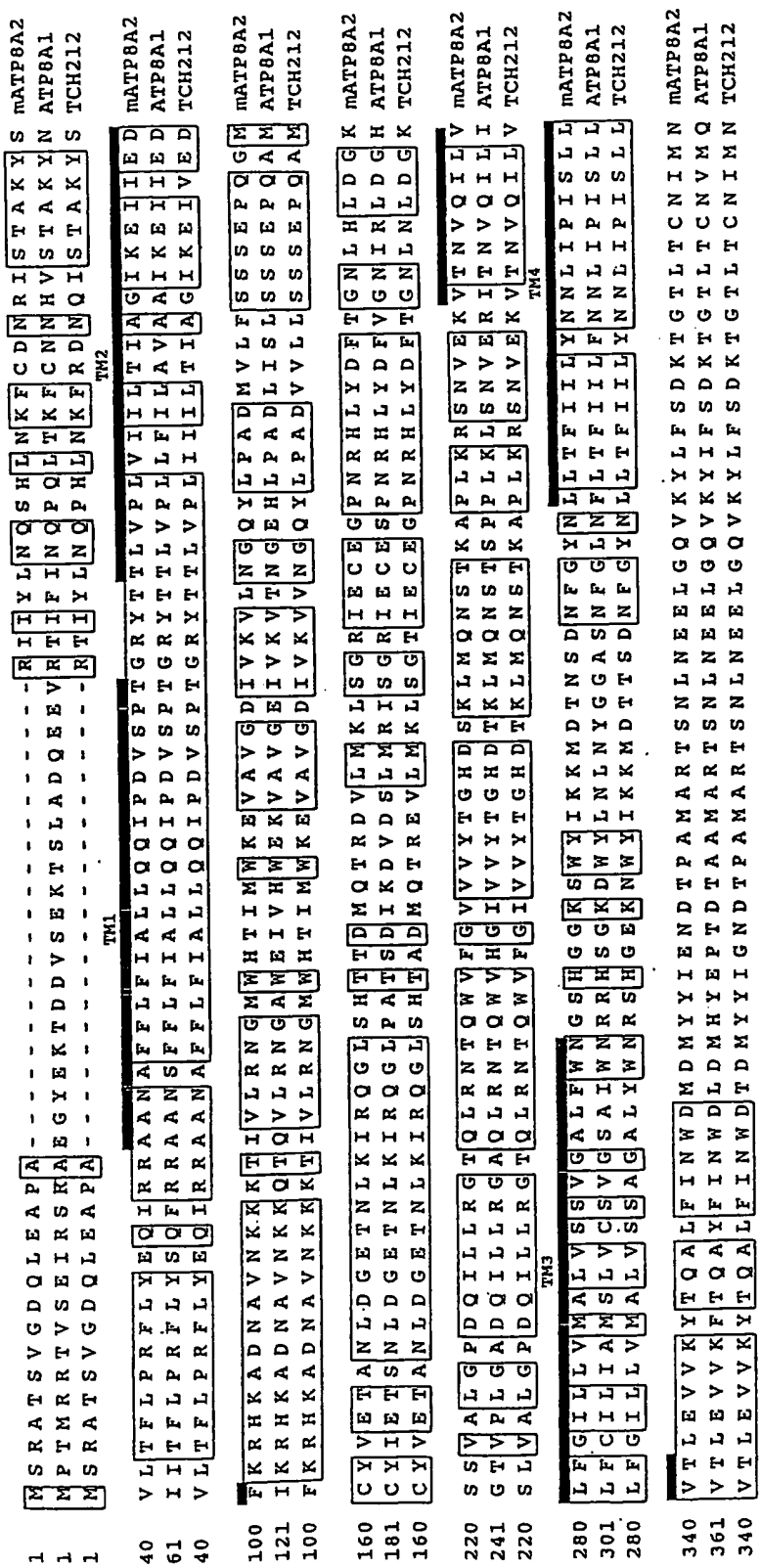


FIG. 9

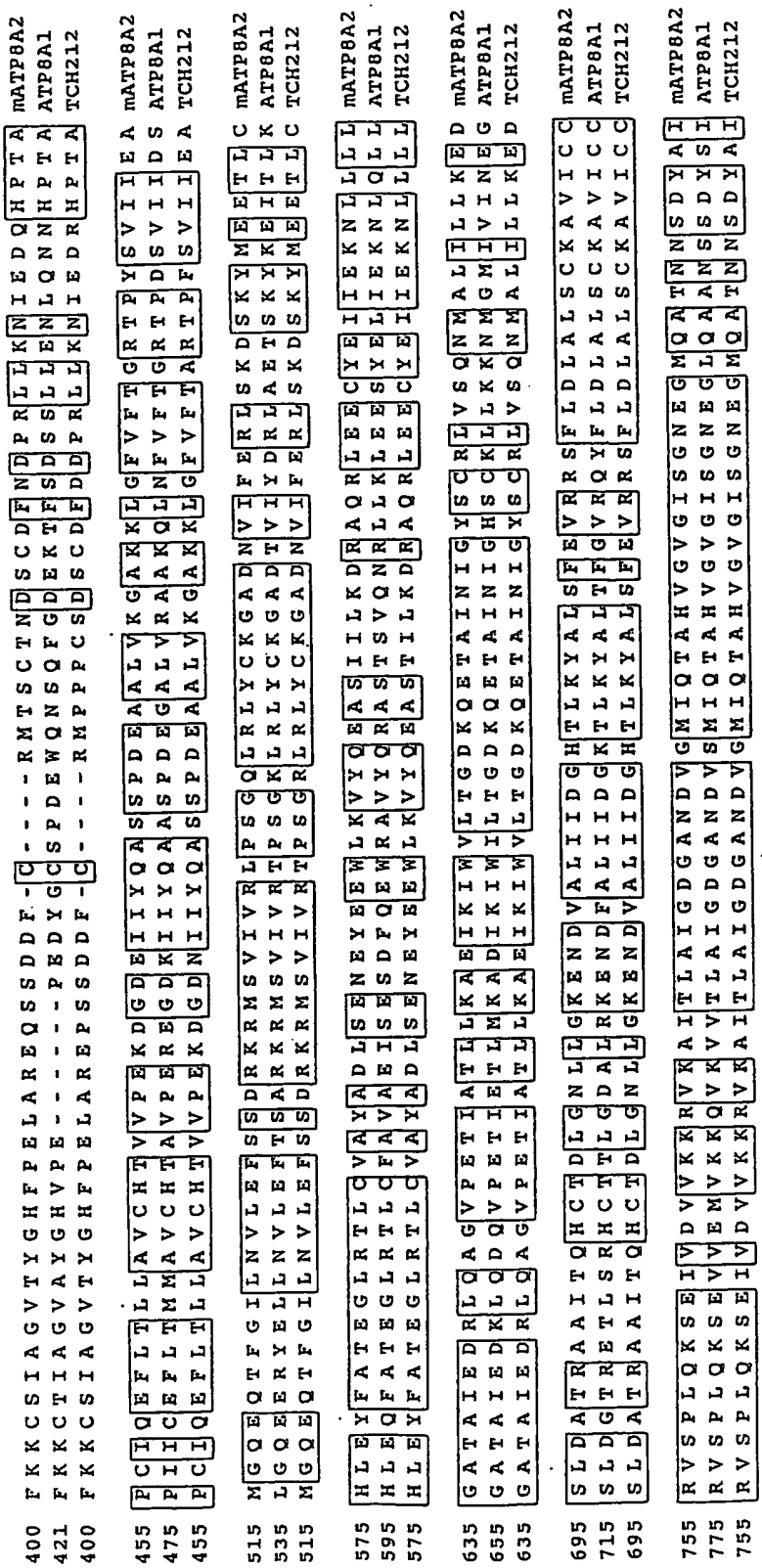

400 FKKCSIAGVTYGHFPELAREQSSDDF-C----RMTSCTNDSCDFNDPRLLKNIEDQHPTA mATP8A2
421 FKKCTIAGVAYGHVPE------PEDYGCSPDEWQNSQFGDDEKTFSDSSLLENLQNNHPTA ATP8A1
400 FKKCSIAGVTYGHFPELAREPSSDDF-C----RMPPPCSDSCDFDDPRLLKNIEDRHPTA TCH212
455 PCIQEFLTLLAVCHTVVPEKDGDEIIYQASSPDEAALVVKGAKKLGFVFTTGRTPYSVIIEA mATP8A2
475 PIICEFLTMMAVCHTAVPEREGDKIIYQAASPDEGALVRAAKQLNFVFTTGRTPDSVIIDS ATP8A1
455 PCIQEFLTLLAVCHTVVPEKDGDNIIYQASSPDEAALVVKGAKKLGFVFTTARTPFSVIIEA TCH212
515 MGQEQTFGILNVLEFSSDRKRMSVIVRLPSGQLRLYCKGADNVIFERLSKDSKYMEETLC mATP8A2
535 LGQEERYELLNVLEFTSARKRMSVIVRTPSGKLRLYCKGADTVIYDRLAETSKYKEITLK ATP8A1
515 MGQEQTFGILNVLEFSSDRKRMSVIVRTPSGRLRLYCKGADNVIFERLSKDSKYMEETLC TCH212
575 HLEYFATEGLRTLCVAYADLSENEYEEWLKVYQEASIILKDRAQRLEECYEIIEKNLLLLL mATP8A2
595 HLEQFATEGLRTLCFAVAEISEESDFQEWRAVYQRASTSVQNRLLKLEESYELIEKNLQLL ATP8A1
575 HLEYFATEGLRTLCVAYADLSENEYEEWLKVYQEASTILKDRAQRLEECYEIIEKNLLLLL TCH212
635 GATAIEDRLQAGVPETIATLLKAEIKIWVLTGDKQETAINIGYSCRLVSQNMALILLKEDD mATP8A2
655 GATAIEDKLQDQVPETIETLMKADIKIWILTGDKQETAINIGHSCKLLKKNMGMIVINEGD ATP8A1
635 GATAIEDRLQAGVPETIATLLKAEIKIWVLTGDKQETAINIGYSCRLVSQNMALILLKEDD TCH212
695 SLDATRAAITQHCTDLGNLLGKENDVALIIDGHTLKYALSFEVRRSFLDLALSCKAVICC mATP8A2
715 SLDGTRETLSRHCTTLGDALRKENDFALIIDGKTLKYALTFGVRQYFLDLALSCKAVICC ATP8A1
695 SLDATRAAITQHCTDLGNLLGKENDVALIIDGHTLKYALSFEVRRSFLDLALSCKAVICC TCH212
755 RVSPLQKSEIVDVVKKRVKAITLAIGDGANDVGMIQTAHVGVGISGNEGMQATNNSDYAII mATP8A2
775 RVSPLQKSEVVEMVKKQVKVVTLAIGDGANDVSMIQTAHVGVGISGNEGLQAANSSDYSII ATP8A1
755 RVSPLQKSEIVDVVKKRVKAITLAIGDGANDVGMIQTAHVGVGISGNEGMQATNNSDYAII TCH212

FIG. 10

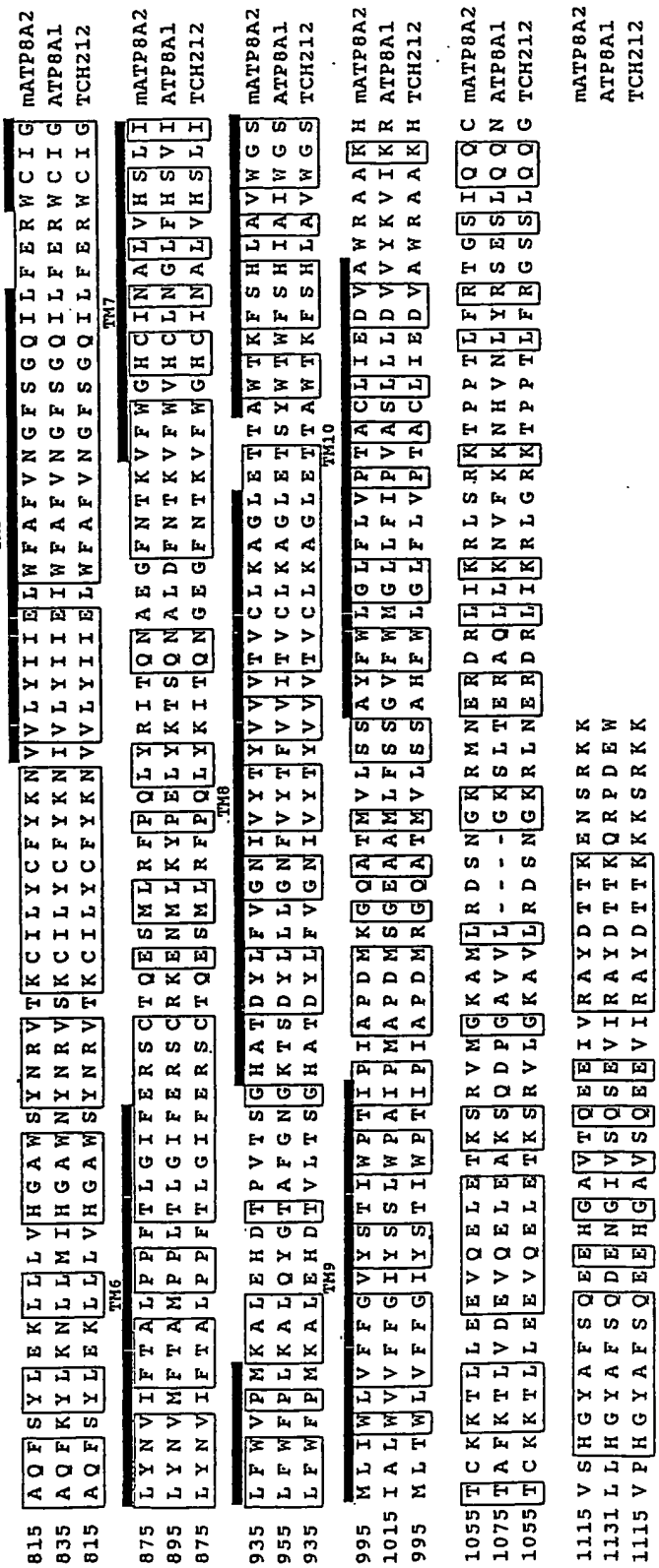


FIG. 11

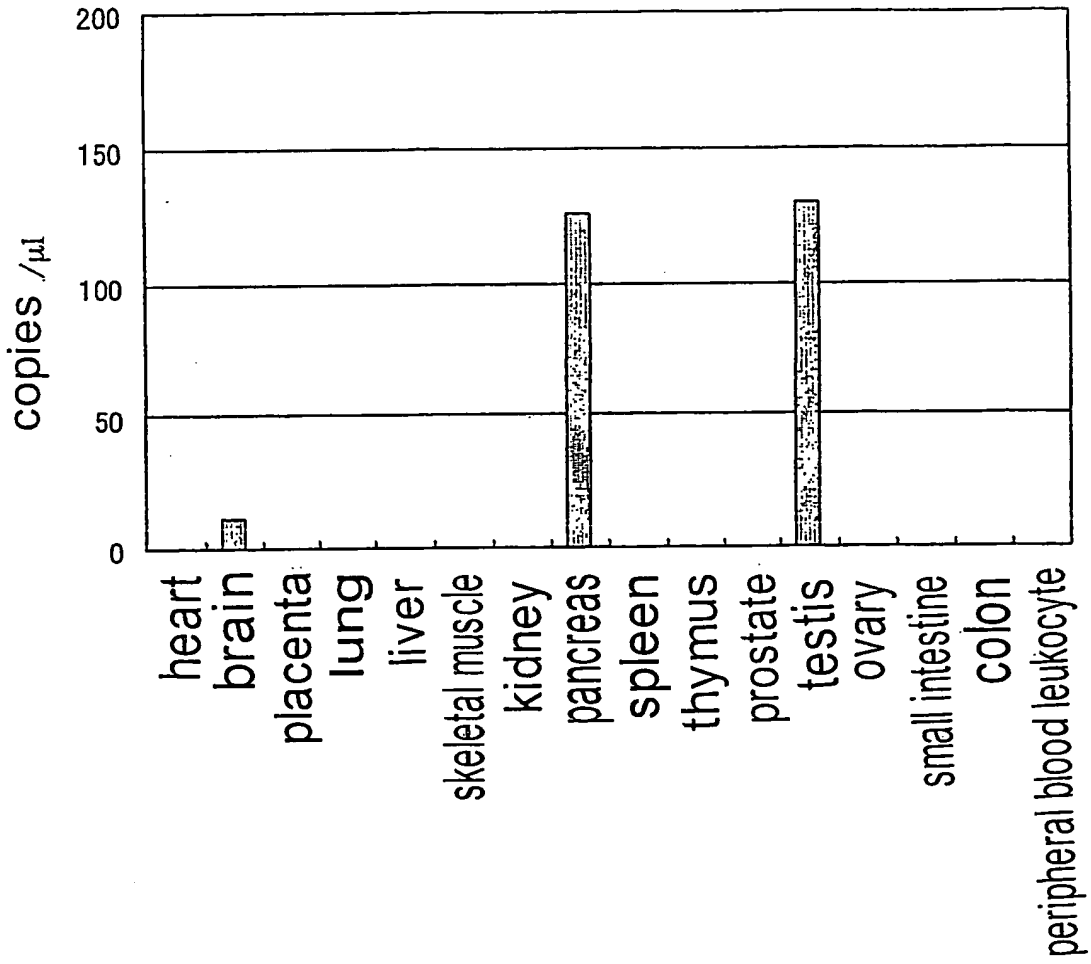

copies /μl
200
150
100
50
0
heart
brain
placenta
lung
liver
skeletal muscle
kidney
pancreas
spleen
thymus
prostate
testis
ovary
small intestine
colon
peripheral blood leukocyte

FIG. 12

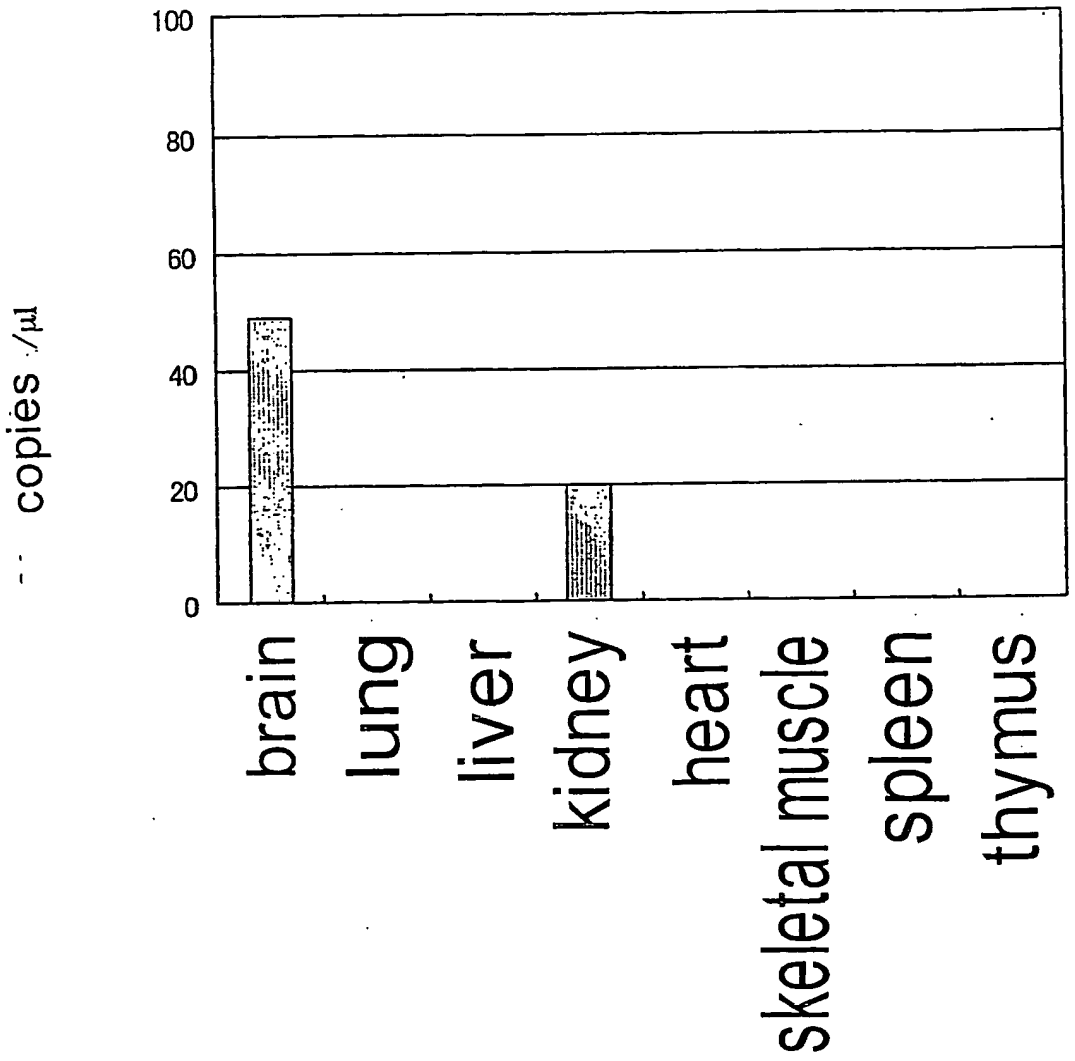

100
80
60
40
20
0
copies /μl
brain
lung
liver
kidney
heart
skeletal muscle
spleen
thymus

FIG. 13

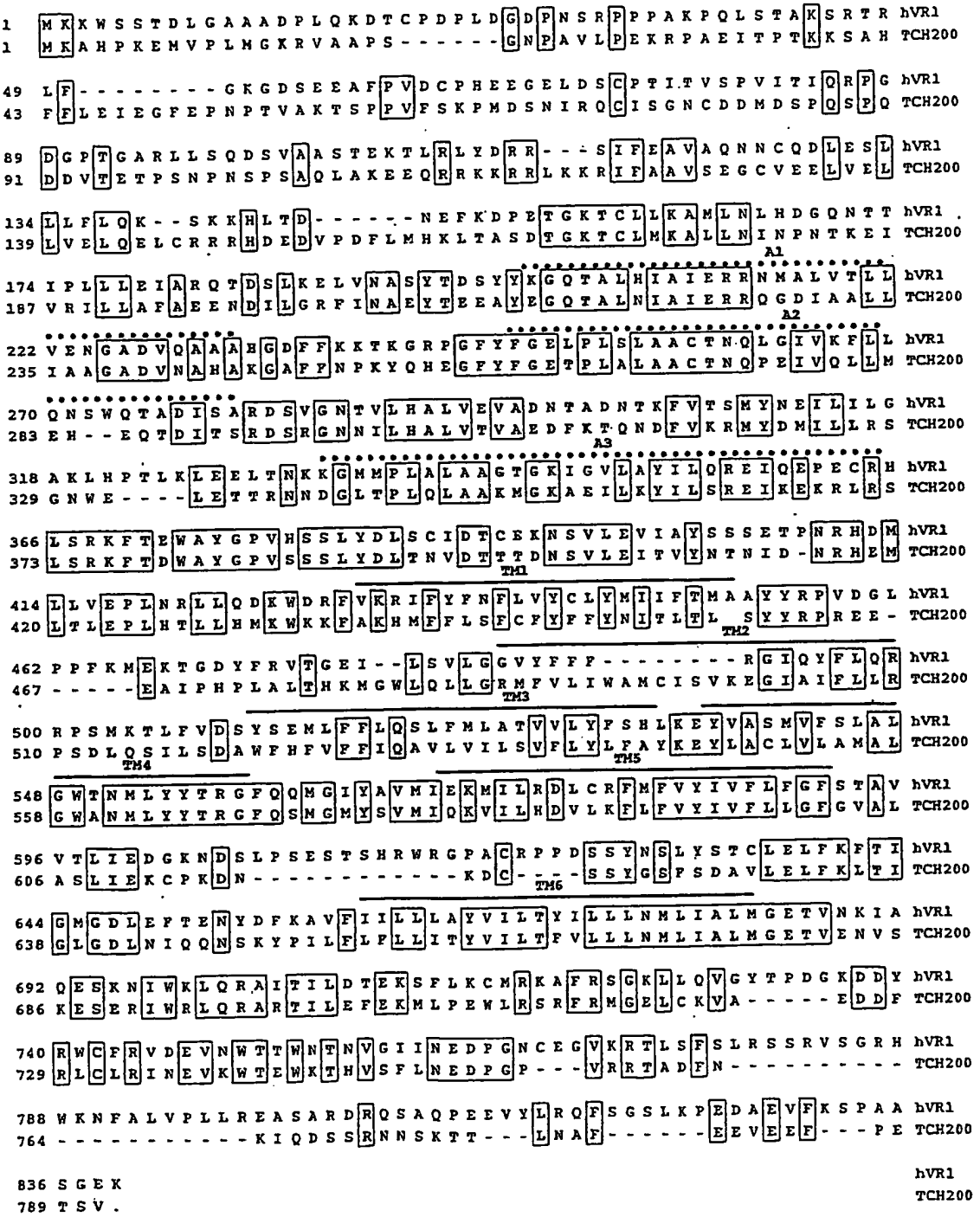


FIG. 14

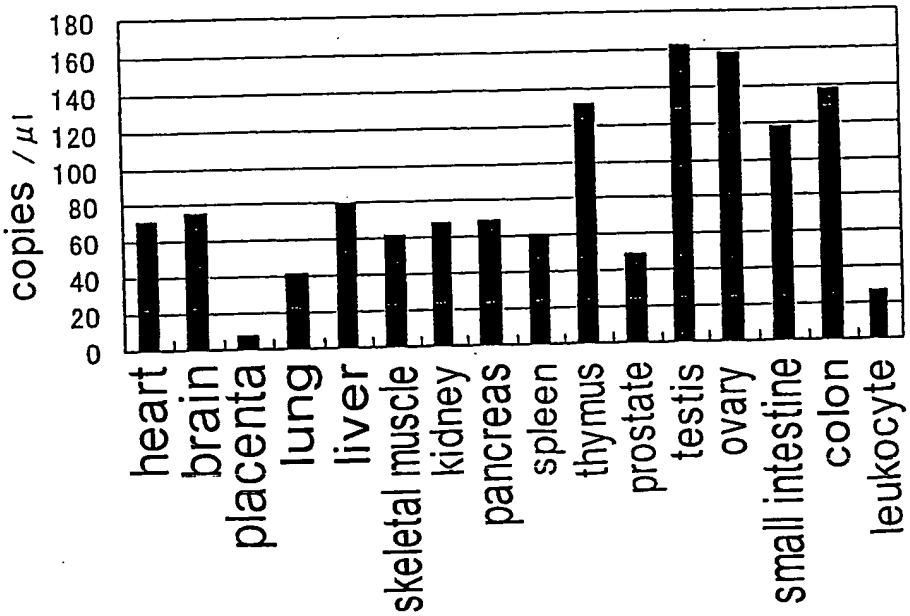

copies /μl
180
160
140
120
100
80
60
40
20
0
heart
brain
placenta
lung
liver
skeletal muscle
kidney
pancreas
spleen
thymus
prostate
testis
ovary
small intestine
colon
leukocyte

FIG. 15

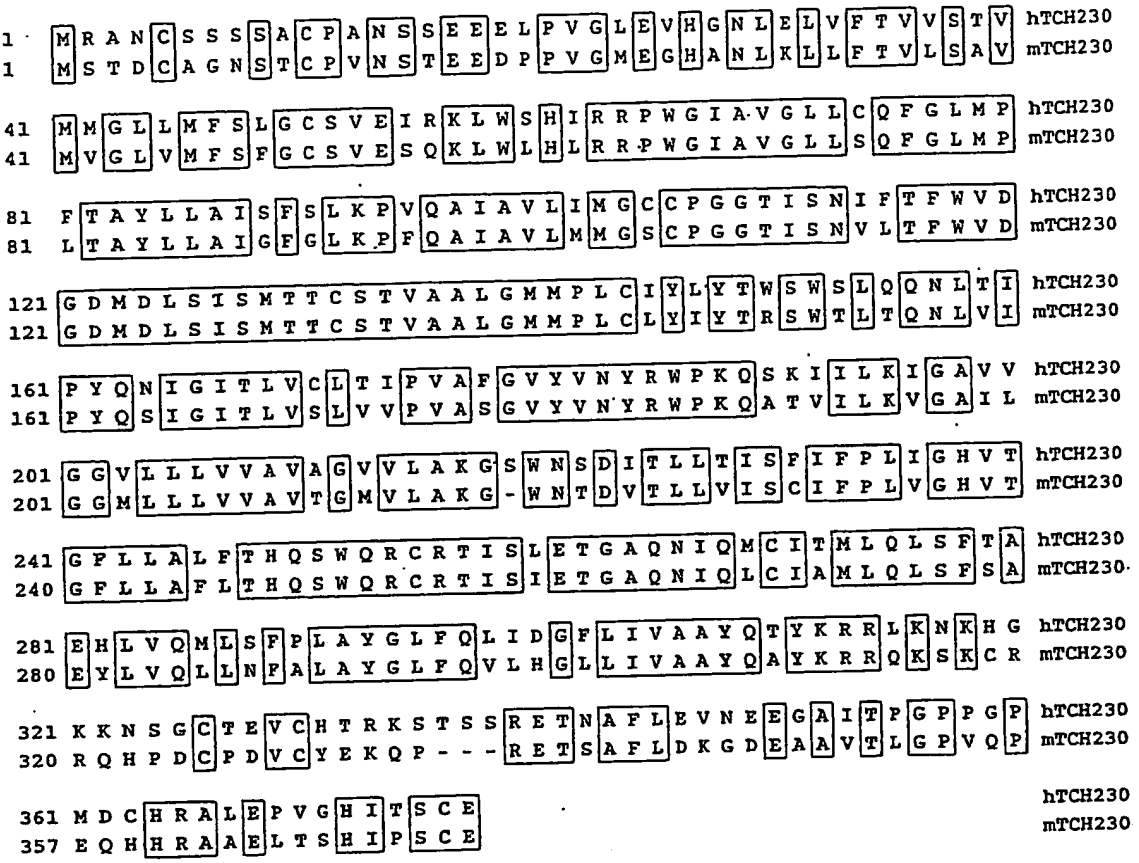

1 MRANCSSSSACPANSSEEELPVGLEVHGNLELVFTVVSTV hTCH230
1 MSTDCAGNSTCPVNSTEEDPPVGMEGHANLKLLFTVLSAV mTCH230
41 MMGLLMFSLGCSVEIRKLWSHIRRPWGIAVGLLCQFGLMP hTCH230
41 MVGLVMFSFGCSVESQKLWLHLRRPWGIAVGLLSQFGLMP mTCH230
81 FTAYLLAISFSLKPVQAIAVLIMGCCPGGTISNIFTFWVD hTCH230
81 LTAYLLAIGFGLKPFQAIAVLMMGSCPGGTISNVLTFWVD mTCH230
121 GDMDLSISMTTCSTVAALGMMPLCIYLYTWSWSLQQNLTI hTCH230
121 GDMDLSISMTTCSTVAALGMMPLCLYIYTRSWTLTQNLVI mTCH230
161 PYQNIGITLVCLTIPVAFGVYVNYRWPKQSKIILKIGAVV hTCH230
161 PYQSIGITLVSLVVPVASGVYVNYRWPKQATVILKVGAIL mTCH230
201 GGVLLLVVAVAGVVLAKGSWNSDITLLTISFIFPLIGHVT hTCH230
201 GGMLLLVVAVTGMVLAKG-WNTDVTLLVISCIFPLVGHVT mTCH230
241 GFLLALFTHQSWQRCRTISLETGAQNIQMCITMLQLSFTA hTCH230
240 GFLLAFLTHQSWQRCRTISIETGAQNIQLCIAMLQLSFSA mTCH230
281 EHLVQMLSFPLAYGLFQLIDGFLIVAAYQTYKRRLKNKHG hTCH230
280 EYLVQLLNFALAYGLFQVLHGLLIVAAYQAYKRRQKSKCR mTCH230
321 KKNSGCTEVCHTRKSTSSRETNAFLEVNEEGAITPGPPGP hTCH230
320 RQHPDCPDVCYEKQP---RETSAFLDKGDEAAVTLGPVQP mTCH230
361 MDCHRALEPVGHITSCE hTCH230
357 EQHHRAAELTSHIPSCE mTCH230

FIG. 16

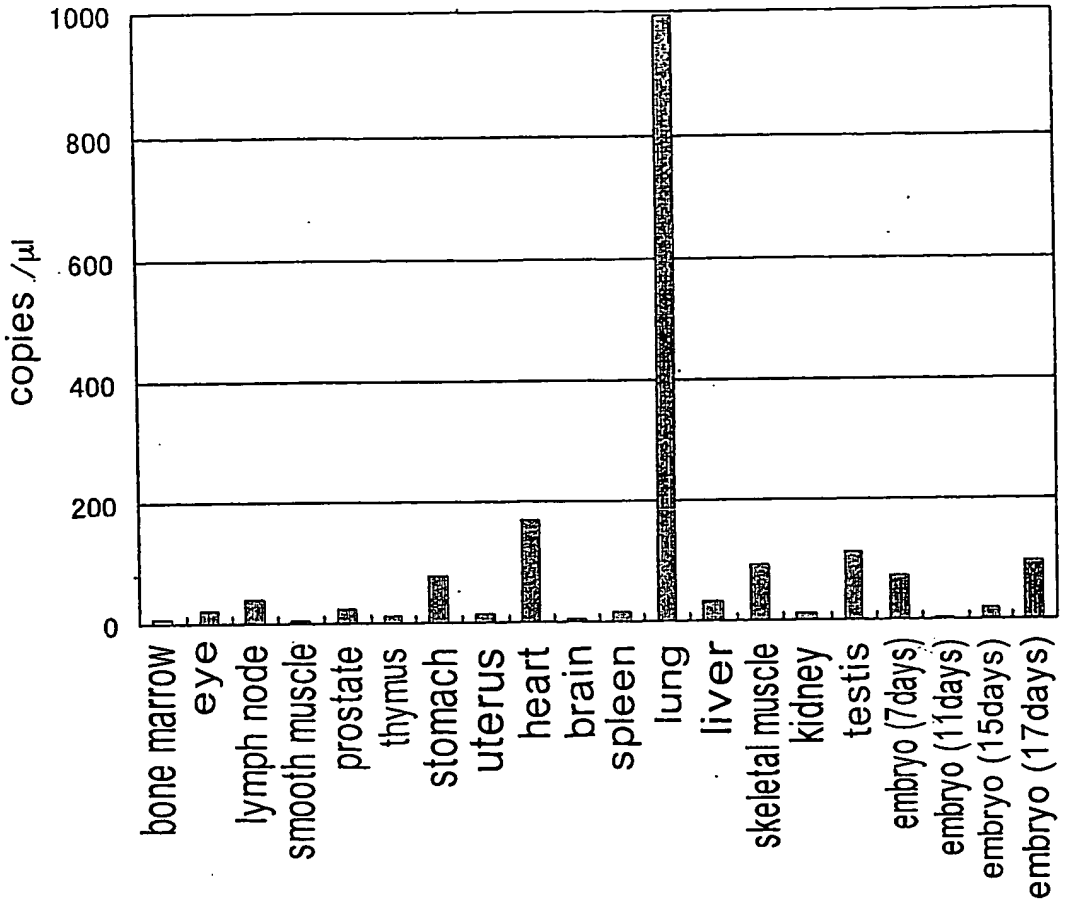

1000
800
600
400
200
0
copies /μl
bone marrow
eye
lymph node
smooth muscle
prostate
thymus
stomach
uterus
heart
brain
spleen
lung
liver
skeletal muscle
kidney
testis
embryo (7days)
embryo (11days)
embryo (15days)
embryo (17days)

FIG. 17

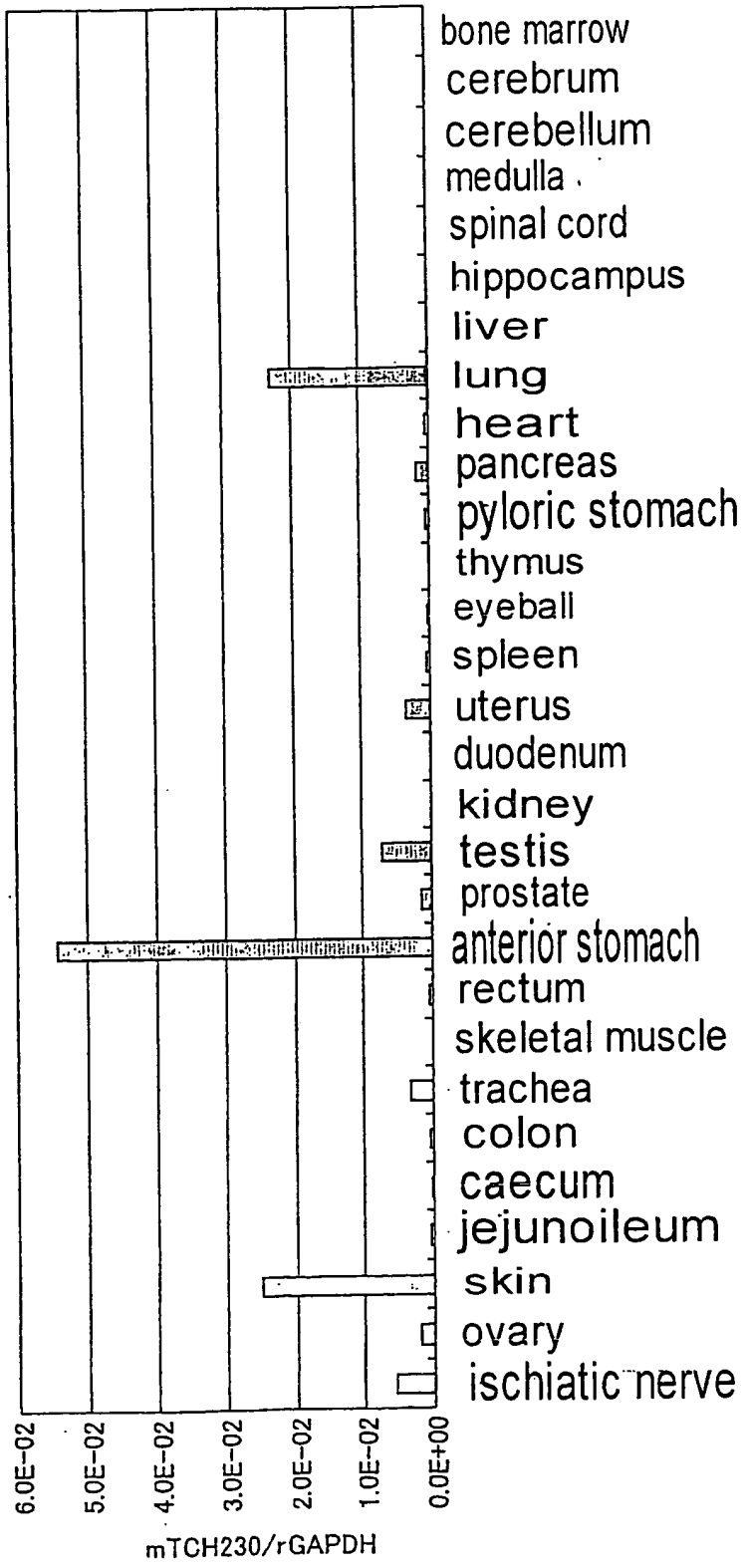

bone marrow
cerebrum
cerebellum
medulla
spinal cord
hippocampus
liver
lung
heart
pancreas
pyloric stomach
thymus
eyeball
spleen
uterus
duodenum
kidney
testis
prostate
anterior stomach
rectum
skeletal muscle
trachea
colon
caecum
jejunoileum
skin
ovary
ischiatic nerve
6.0E-02
5.0E-02
4.0E-02
3.0E-02
2.0E-02
1.0E-02
0.0E+00
mTCH230/rGAPDH

FIG. 18

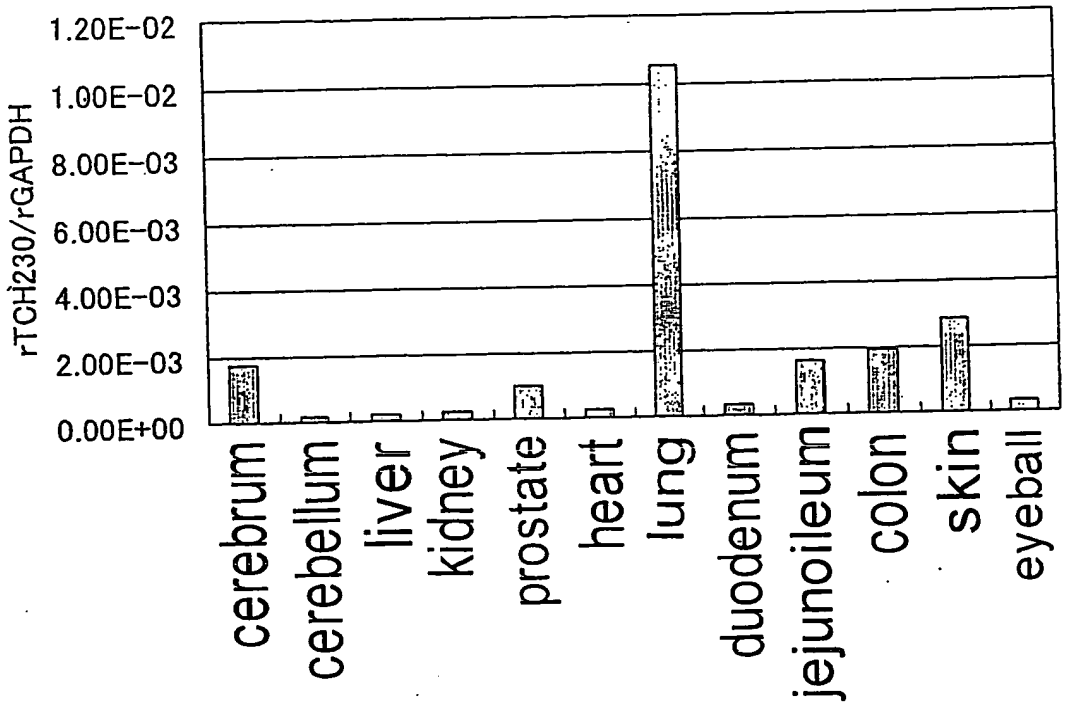

1.20E-02
1.00E-02
8.00E-03
6.00E-03
4.00E-03
2.00E-03
0.00E+00
rTCH230/rGAPDH
cerebrum
cerebellum
liver
kidney
prostate
heart
lung
duodenum
jejunoileum
colon
skin
eyeball

FIG. 19

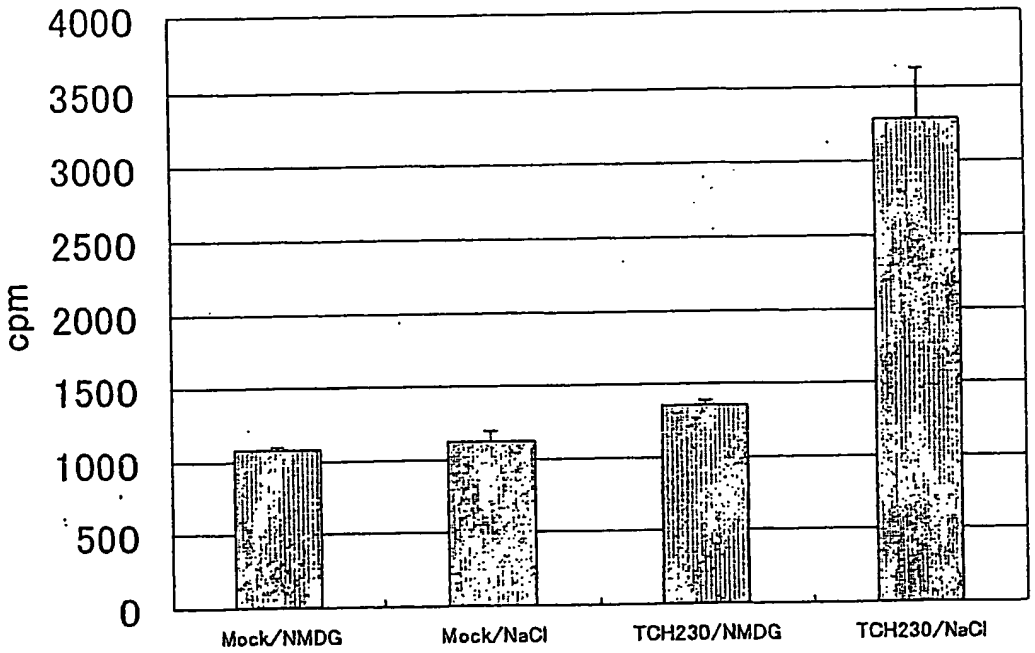

4000
3500
3000
2500
2000
1500
1000
500
0
cpm
Mock/NMDG
Mock/NaCl
TCH230/NMDG
TCH230/NaCl

FIG. 20

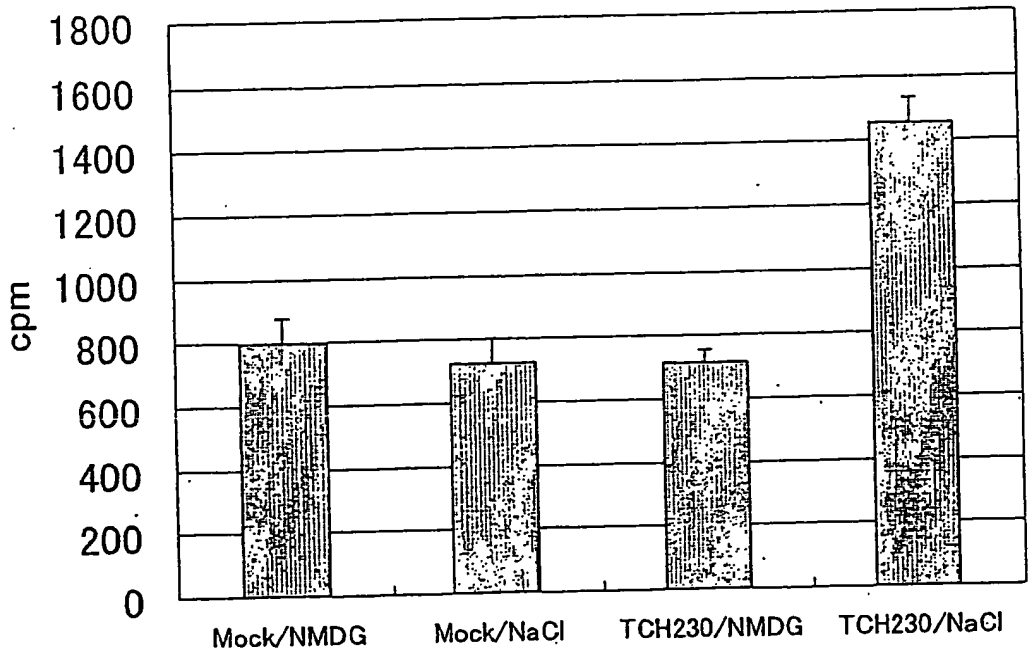

1800
1600
1400
1200
1000
800
600
400
200
0
cpm
Mock/NMDG
Mock/NaCl
TCH230/NMDG
TCH230/NaCl

FIG. 21

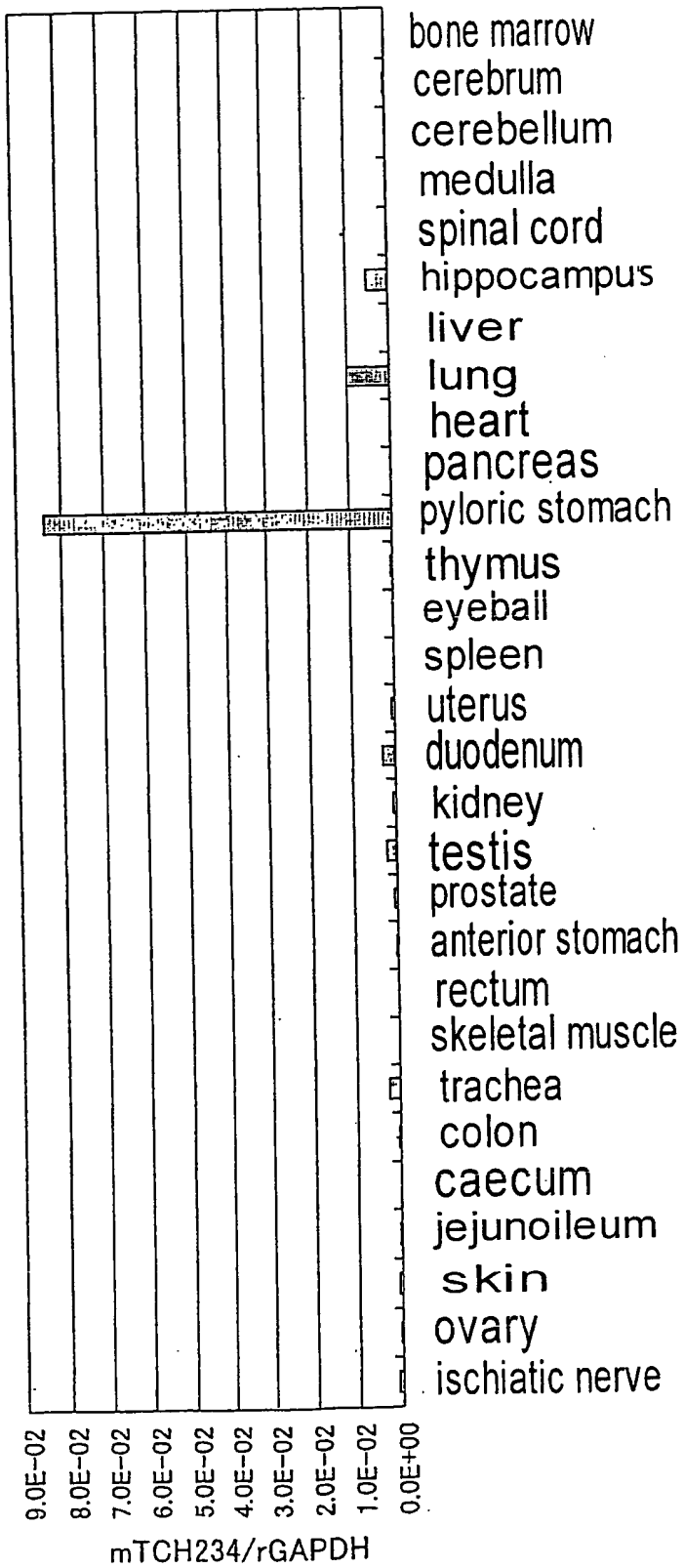

bone marrow
cerebrum
cerebellum
medulla
spinal cord
hippocampus
liver
lung
heart
pancreas
pyloric stomach
thymus
eyeball
spleen
uterus
duodenum
kidney
testis
prostate
anterior stomach
rectum
skeletal muscle
trachea
colon
caecum
jejunoileum
skin
ovary
ischiatic nerve
9.0E-02
8.0E-02
7.0E-02
6.0E-02
5.0E-02
4.0E-02
3.0E-02
2.0E-02
1.0E-02
0.0E+00
mTCH234/rGAPDH

FIG. 22

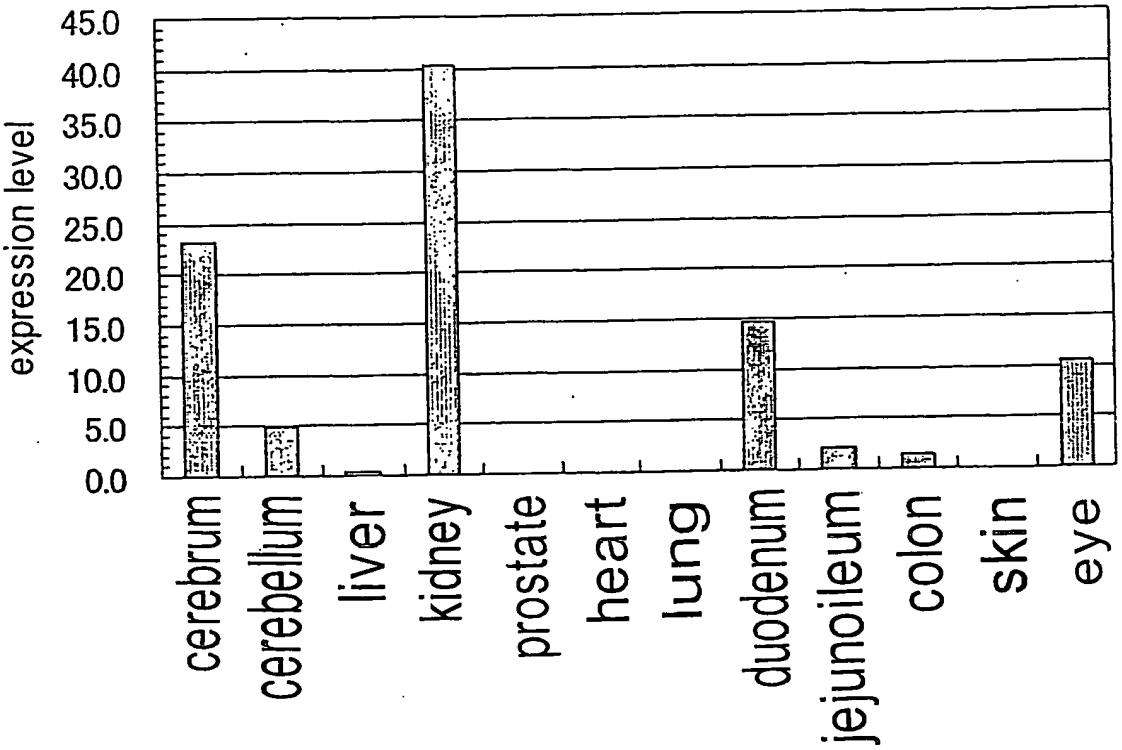

45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
expression level
cerebrum
cerebellum
liver
kidney
prostate
heart
lung
duodenum
jejunoileum
colon
skin
eye

FIG. 23

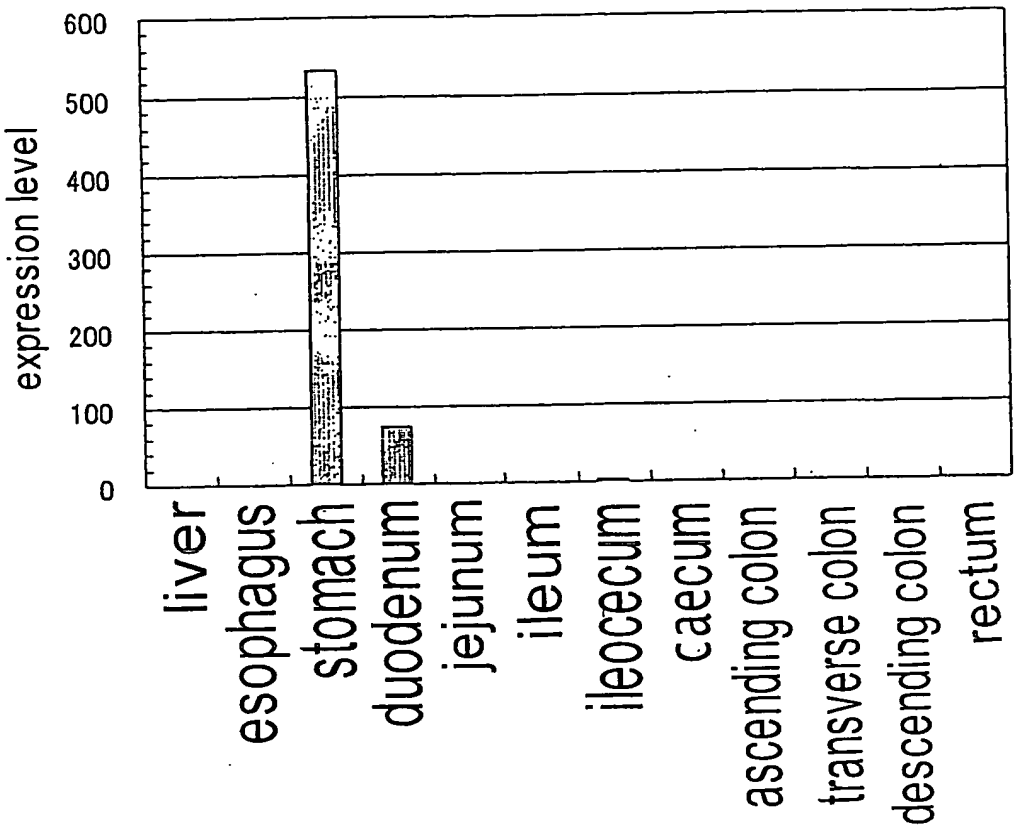

600
500
400
300
200
100
0
expression level
liver
esophagus
stomach
duodenum
jejunum
ileum
ileocecum
caecum
ascending colon
transverse colon
descending colon
rectum

FIG. 24

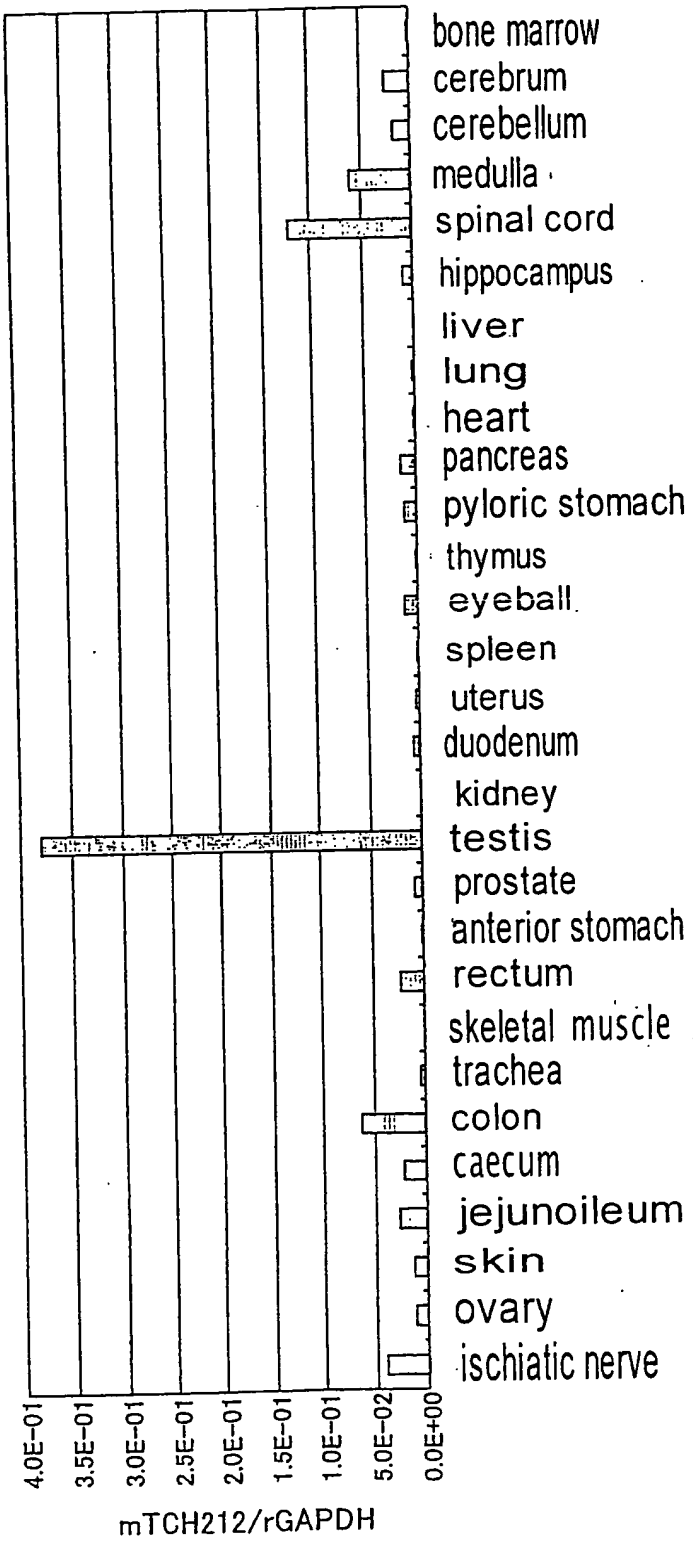

bone marrow
cerebrum
cerebellum
medulla
spinal cord
hippocampus
liver
lung
heart
pancreas
pyloric stomach
thymus
eyeball
spleen
uterus
duodenum
kidney
testis
prostate
anterior stomach
rectum
skeletal muscle
trachea
colon
caecum
jejunoileum
skin
ovary
ischiatic nerve
4.0E-01
3.5E-01
3.0E-01
2.5E-01
2.0E-01
1.5E-01
1.0E-01
5.0E-02
0.0E+00
mTCH212/rGAPDH

FIG. 25

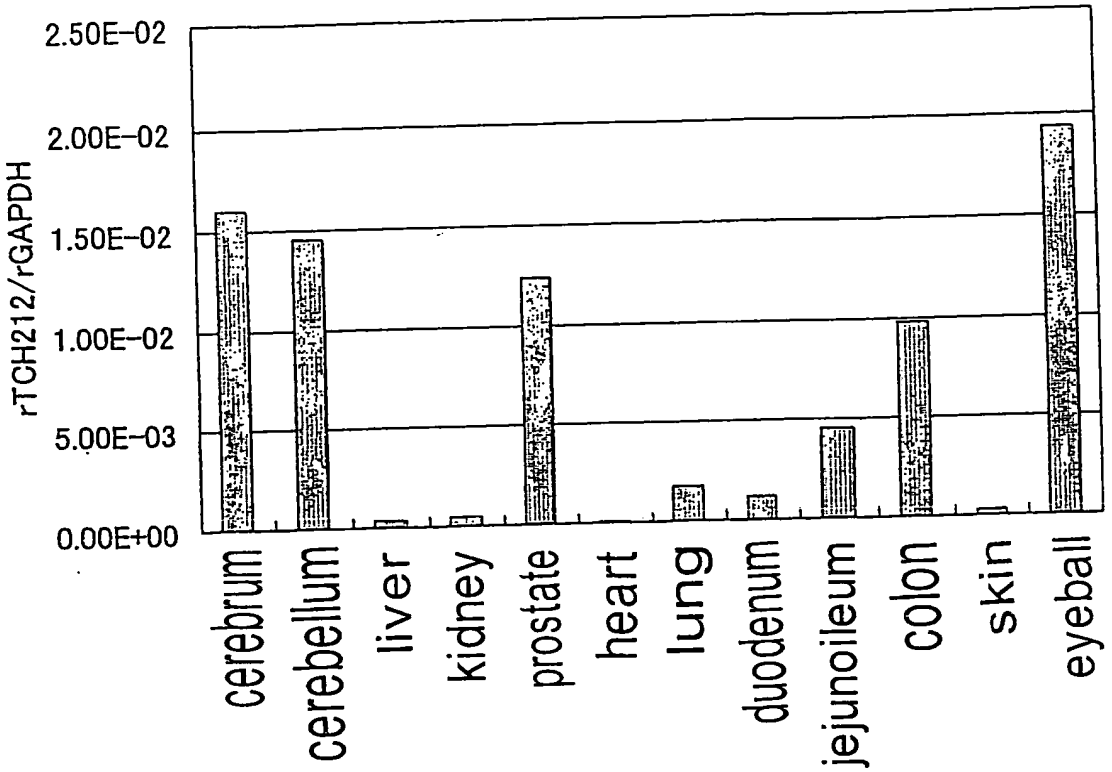

2.50E-02
2.00E-02
1.50E-02
1.00E-02
5.00E-03
0.00E+00
rTCH212/rGAPDH
cerebrum
cerebellum
liver
kidney
prostate
heart
lung
duodenum
jejunoileum
colon
skin
eyeball

FIG. 26

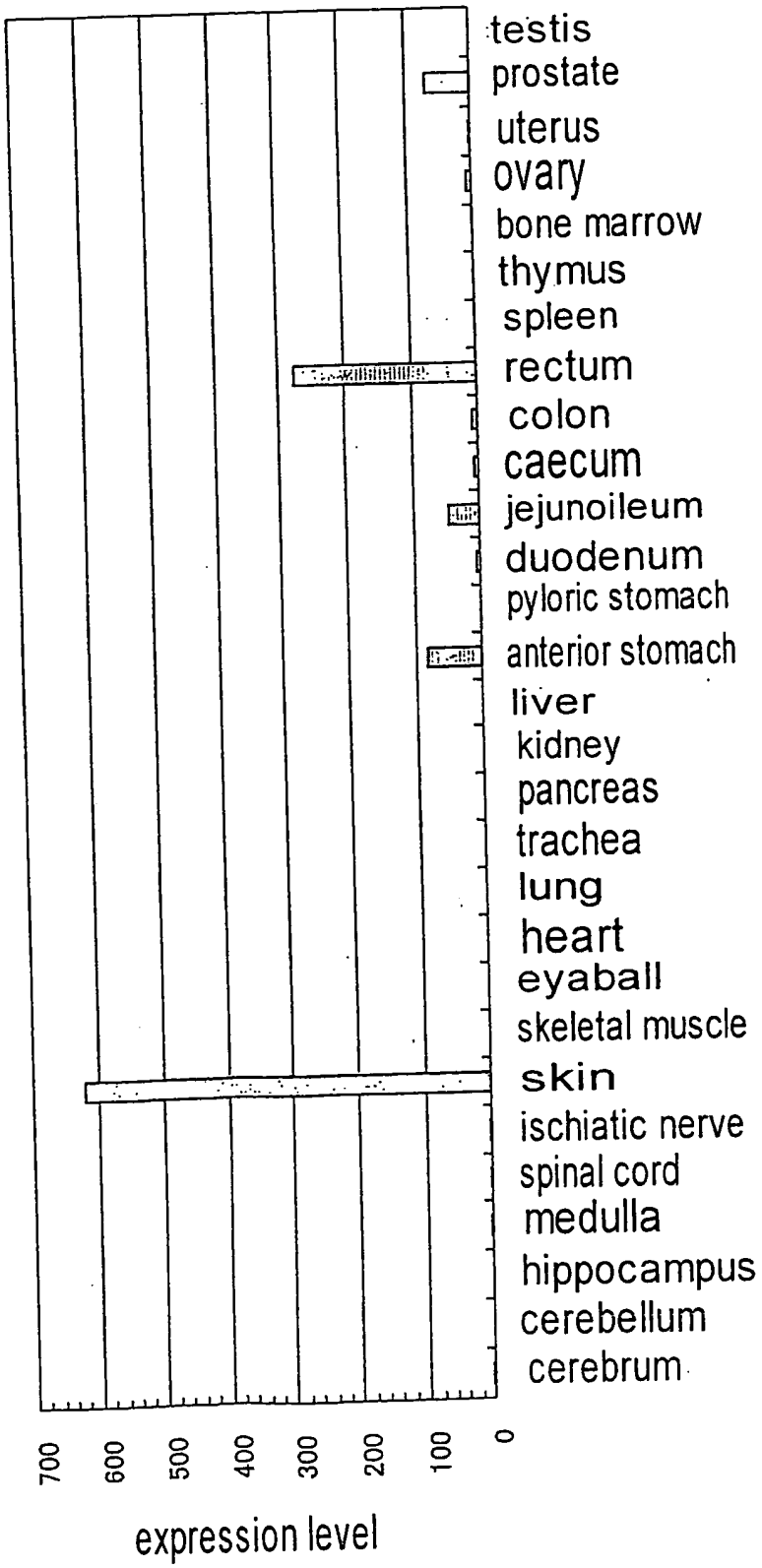

testis
prostate
uterus
ovary
bone marrow
thymus
spleen
rectum
colon
caecum
jejunoileum
duodenum
pyloric stomach
anterior stomach
liver
kidney
pancreas
trachea
lung
heart
eyaball
skeletal muscle
skin
ischiatic nerve
spinal cord
medulla
hippocampus
cerebellum
cerebrum
700
600
500
400
300
200
100
0
expression level

FIG. 27

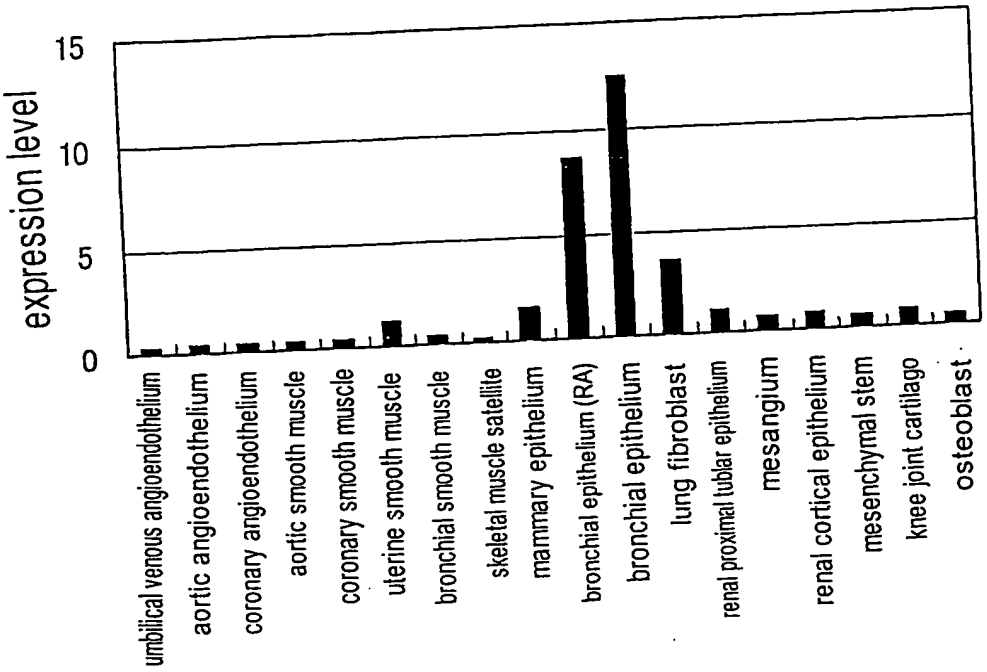

expression level
15
10
5
0
umbilical venous angioendothelium
aortic angioendothelium
coronary angioendothelium
aortic smooth muscle
coronary smooth muscle
uterine smooth muscle
bronchial smooth muscle
skeletal muscle satellite
mammary epithelium
bronchial epithelium (RA)
bronchial epithelium
lung fibroblast
renal proximal tublar epithelium
mesangium
renal cortical epithelium
mesenchymal stem
knee joint cartilago
osteoblast

FIG. 28

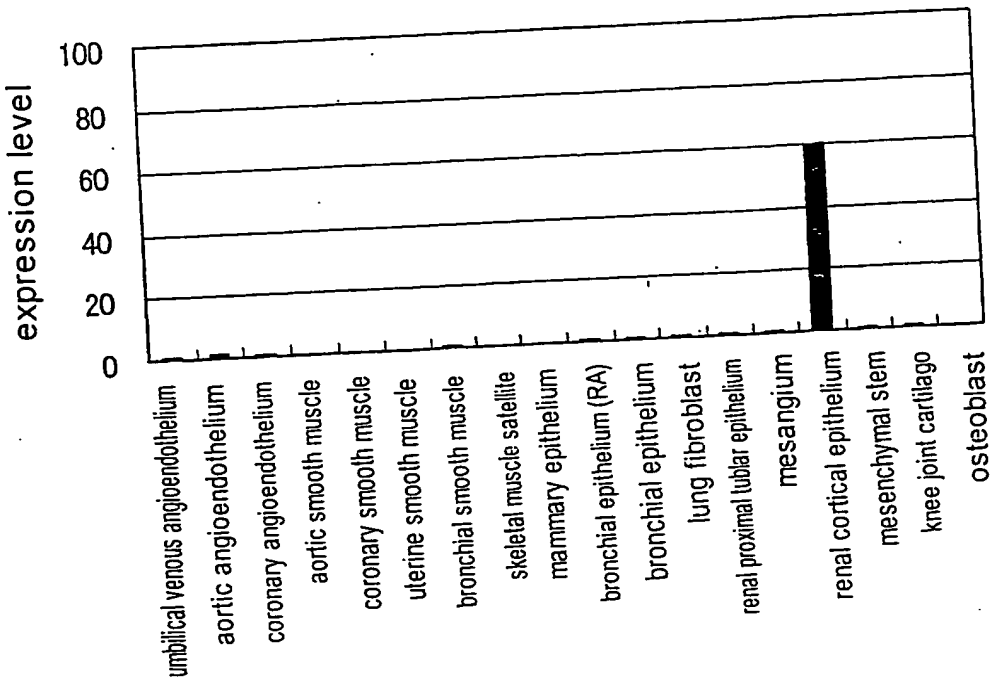

expression level
100
80
60
40
20
0
umbilical venous angioendothelium
aortic angioendothelium
coronary angioendothelium
aortic smooth muscle
coronary smooth muscle
uterine smooth muscle
bronchial smooth muscle
skeletal muscle satellite
mammary epithelium
bronchial epithelium (RA)
bronchial epithelium
lung fibroblast
renal proximal tublar epithelium
mesangium
renal cortical epithelium
mesenchymal stem
knee joint cartilago
osteoblast

FIG. 29

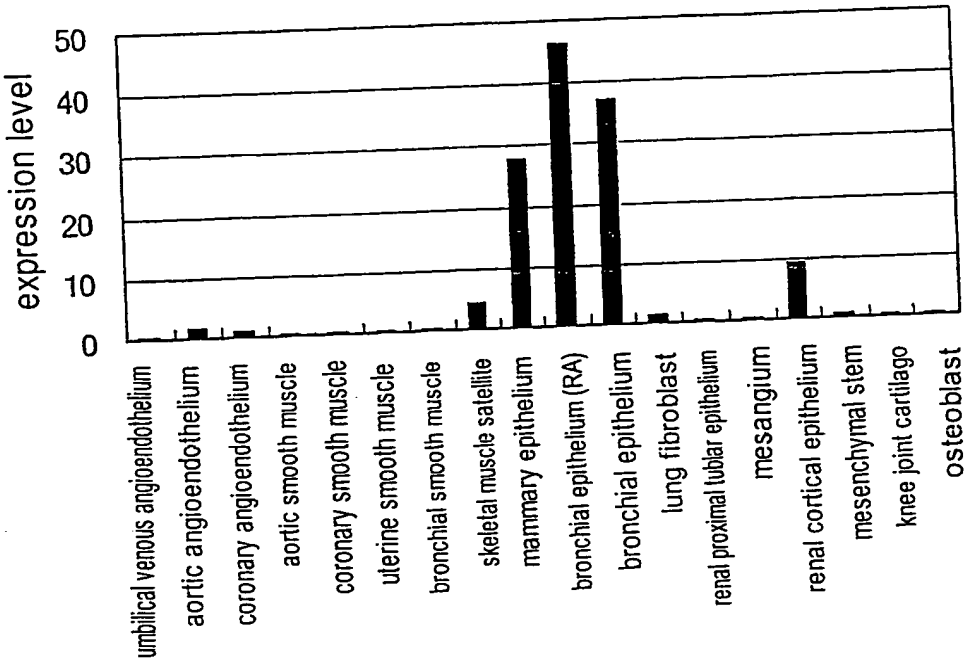

expression level
50
40
30
20
10
0
umbilical venous angioendothelium
aortic angioendothelium
coronary angioendothelium
aortic smooth muscle
coronary smooth muscle
uterine smooth muscle
bronchial smooth muscle
skeletal muscle satellite
mammary epithelium
bronchial epithelium (RA)
bronchial epithelium
lung fibroblast
renal proximal tubular epithelium
mesangium
renal cortical epithelium
mesenchymal stem
knee joint cartilago
osteoblast

FIG. 30

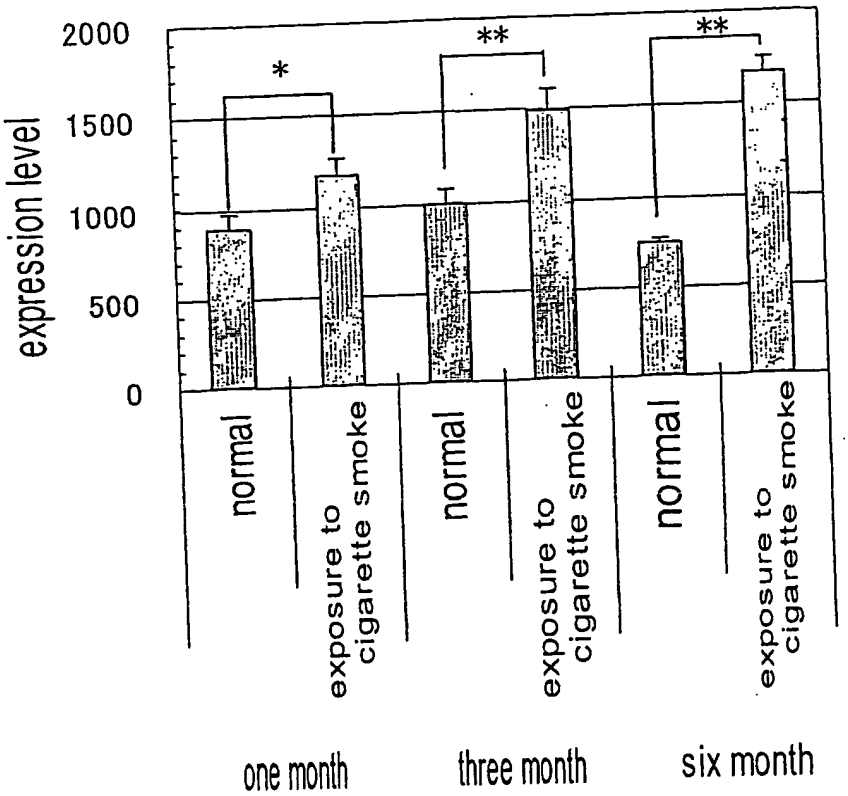

2000
1500
1000
500
0
expression level
*
**
**
normal
exposure to cigarette smoke
normal
exposure to cigarette smoke
normal
exposure to cigarette smoke
one month
three month
six month

FIG. 31

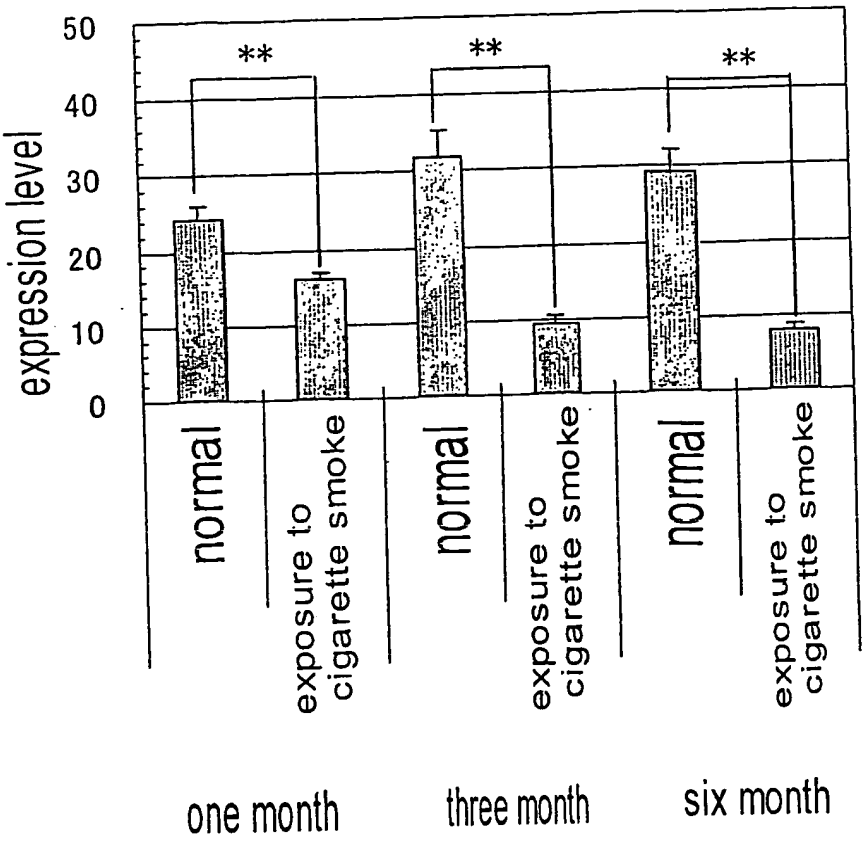

50
40
30
20
10
0
expression level
**
**
**
normal
exposure to cigarette smoke
normal
exposure to cigarette smoke
normal
exposure to cigarette smoke
one month
three month
six month

FIG. 32

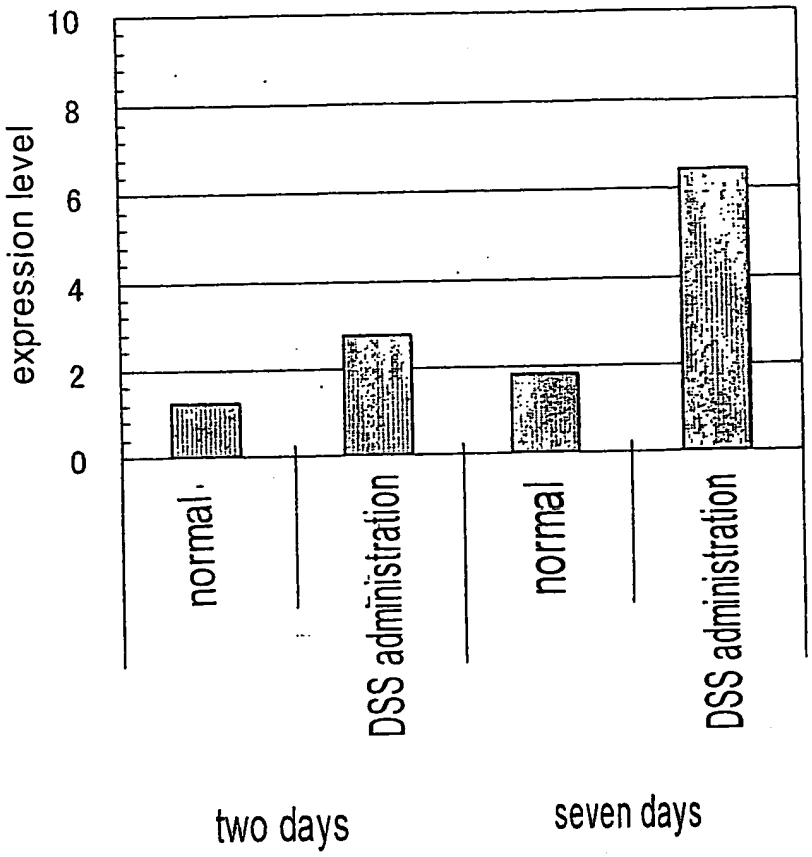
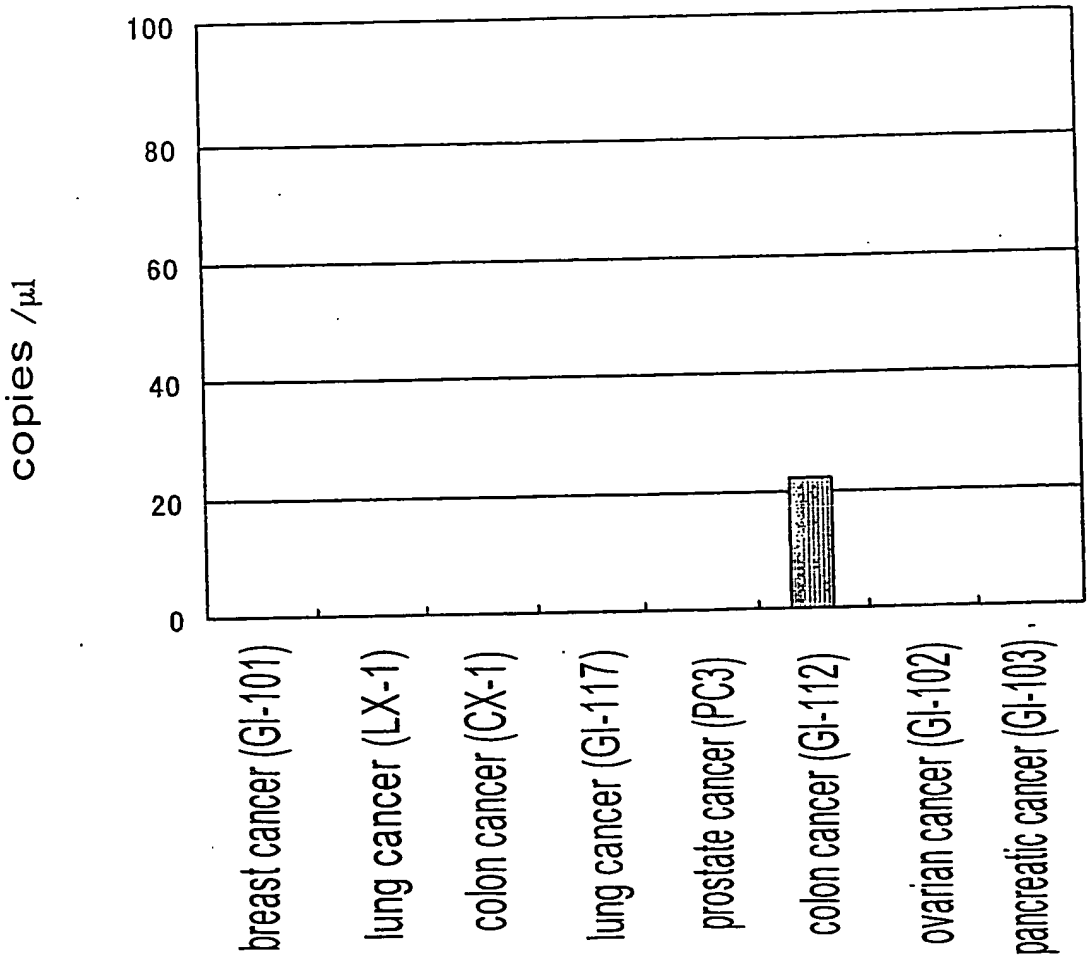

10
8
6
4
2
0
expression level
normal
DSS administration
normal
DSS administration
two days
seven days

FIG. 33


copies /μl
100
80
60
40
20
0
breast cancer (GI-101)
lung cancer (LX-1)
colon cancer (CX-1)
lung cancer (GI-117)
prostate cancer (PC3)
colon cancer (GI-112)
ovarian cancer (GI-102)
pancreatic cancer (GI-103)